REMARKS

Status of the Claims and Explanation of the Amendments

Fifty-one (51) claims were originally filed in this case, and four claims (claims 52-55) were added during Applicants' response to the election/restriction requirement filed on August 9, 2006. In the Office Action of October 23, 2006, the Examiner maintained the election/restriction requirement and now claims 12-41, 47-51, and 53-55 are considered withdrawn. The claims currently under examination are claims 1-11, 42-46, and 52.

Claim Rejections:

Claim 52 is rejected under 35 U.S.C. § 112, ¶ 1, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors(s), at the time the application was filed, had possession of the invention.

Claims 2-4, 7, 8, 45, and 46 are rejected under 35 U.S.C. § 112, ¶ 2, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1, 5, 6, 11, and 42-44 stand rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Michon et al. (In: Streptococci and the Host. (Ed) Horaud et al., Plenum Press, New York, pages 847- 850, 1997) (hereafter "Michon '97").

Claims 1, 2, 5, 6, 10, 11, and 42-44 are rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Paoletti et al. (Infect. Immun. 62:3234-3243, 1994) (hereafter "Paoletti").

Claims 9 and 52 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Paoletti, in view of Wang et al. (PNAS 95: 6584-6589, 1998) (hereafter "Wang").[1]

Claims 2, 3, 7, 8, 45, and 46 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Michon '97, in view of U.S. Patent No. 6,602,508 (hereafter "Michon '508") and Laude-Sharp et al. (In: Abstracts of the 97th General Meeting of the American Society for Microbiology, Miami Beach, FL, page 251, #E-62, 1997) (hereafter "Laude-Sharp").

Claims 1-7 and 42-45 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,993,825 to Jennings ("Jennings"), in view of Paoletti and Claesson et al. (J. Pediatr. 114: 970199, 1989) (hereafter "Claesson").

Claim Objections:

The Examiner has objected to claim 8 for lacking a period at the end of the claim, and to claim 42 for reciting "multiv alent". In this paper, Applicants have amended the claims to correct these typographical errors.

Claim Amendments:

In this paper, Applicants have amended claim 1. Claim 1 now recites the following:

[1] Applicants note here that the pending Office Action actually rejects claims 9 and 52 under 35 U.S.C. § 102(b) for being "anticipated" by Paoletti in view of Wang, rather than under 35 U.S.C. § 103(a). However, given the Examiner's remarks made in connection with the rejection, as well as the fact that the rejection is under the part of the Office Action entitled "Rejection(s) under 35 U.S.C. § 103", it Applicants' understanding that the rejection of claims 9 and 52 was intended to be made under 35 U.S.C. § 103(a). Thus, Applicants have addressed the rejection of these claims herein assuming that the rejection is under 35 U.S.C. § 103(a).

> 1. A multivalent conjugate molecule comprising carrier protein covalently linked to polysaccharides, wherein said polysaccharides comprise at least three different types of purified bacterial capsular polysaccharide , wherein said at least three different types of purified bacterial capsular polysaccharide are obtained by treating bacteria with an enzyme or base, directly followed by separation, and wherein the molecule elicits protective antibodies.

Support for the amendments to claim 1 is found throughout the specification (e.g., see specification, ¶¶ [55] and [56]). Applicants respectfully submit that no new matter has been added by these amendments.

Applicants have also amended claims to address the rejections under 35 U.S.C. § 112. The details of the amendments are provided in the next section.

Rejections under 35 U.S.C. § 112

A. Rejection under 35 U.S.C. § 112, ¶ 1

Applicants respectfully traverse the rejection of claim 52 under 35 U.S.C. § 112, ¶ 1 for allegedly containing new matter. The Examiner contends that paragraph [41] of Applicants' specification does not provide support for this claim, notwithstanding Applicants' previous statements to the contrary.

In this paper, Applicants have amended claim 52 to recite, *inter alia*, that the polysaccharides are "purified polysaccharides". Claim 52 now reads as follows:

> 52. The conjugate molecule of claim 1, wherein the polysaccharides are purified polysaccharides that are less than 100 kilodaltons in molecular weight.

Support for the definition of the term "purified polysaccharides" is given in paragraph [41] of Applicants' specification. Support for the use of "purified polysaccharides" in the conjugate vaccines of the invention is given generally throughout the specification [e.g., see paragraph [49] of Applicants' specification]. Moreover, Applicants maintain that the portion of the claim that recites that the "polysaccharides are less than 100 kilodaltons in molecular weight" also finds support in paragraph [41]. Specifically, the second sentence of paragraph [41] reads as follows:

> In particular, purified oligosaccharide, or bacterial capsular polysaccharide, is substantially free of intact polysaccharide capsule, or fragments of it having molecular weight above 100,000. [specification, paragraph [41], emphasis added].

The portion of the specification recited above clearly supports the reference to the use of purified polysaccharides having a molecular weight less than 100 kD.

For this reason, Applicants respectfully request reconsideration and withdrawal of the new matter rejection of claim 52.

B. Rejections under 35 U.S.C. § 112, ¶ 2

Claims 2-4, 7, 8, 45, and 46 currently stand rejected under 35 U.S.C. § 112, ¶ 2. Applicants' respectfully request reconsideration and withdrawal of the rejection of these claims, in view of the following:

(a) The Examiner states that claims 2-4 are "vague, indefinite, confusing, and appear to lack proper antecedent basis in the limitations 'different bacterial capsular polysaccharides'" [Office Action, page 5]. In response, Applicants have amended the claims. For example, claim 2 now reads, *inter alia*, "The conjugate molecule of claim 1 comprising a

total of four different bacterial capsular polysaccharides...". Applicants respectfully submit that the addition of the phrase "a total of" makes it clear that the "four different bacterial capsular polysaccharides" include the "at least three different bacterial capsular polysaccharides" as claimed in claim 1. Similar amendments have been made to claims 3 and 4.

(b) The Examiner states that claims 7 and 45 are indefinite, because claim 7 recites "type 1a" while claim 45 recites "type Ia". In response, Applicants have amended claim 7 so that it recites "type Ia". Support for this amendment is found, for example, in paragraph [07] of Applicants' specification.

(c) The Examiner states that claims 8 and 46 are indefinite because they depend from claims 7 and 45, respectively, which are rejected for being indefinite as noted above. In view of the amendment to claim 7, however, Applicants respectfully assert that this rejection is moot.

On the basis of the foregoing amendments are remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 2-4, 7, 8, 45, and 46 under 35 U.S.C. § 112, ¶ 2.

Rejections under 35 U.S.C. § 102

A. Rejection of Claims 1, 5, 6, 22, and 42-44 over Michon '97

Applicants' respectfully traverse the rejection of claims 1, 5, 6, 22, and 42-44 under 35 U.S.C. § 102(b) as allegedly being anticipated by Michon '97. Briefly, Michon '97 does not disclose all of the claim elements of Applicants' claims. Accordingly, the rejection should be withdrawn. MPEP § 2131.

Michon '97 is directed to combination conjugate vaccines against multiple serotypes of group B streptococci. According to the Examiner, Michon '97 discloses "a multivalent conjugate vaccine...comprising a beta C protein carrier or tetanus toxoid protein carrier with at least three different Group B Streptococcus capsular polysaccharides from types Ia, II, and III conjugated [thereto]...".

Applicants respectfully disagree with the Examiner's characterization of Michon '97. Whereas the multivalent conjugate molecule claimed by Applicants contains "at least three different bacterial capsular polysaccharides" that are linked to the same carrier protein molecule, the type Ia, II, and III conjugates described by Michon '97 are linked to different carrier protein molecules which may be of the same type. This can be seen, for example, in the first sentence of Section 3:

> The GBS TT conjugates contained 79%, 68%, and 39% CPS by mass for the Ia, II, and III conjugates, respectively, while their beta C conjugate counterparts contained 81%, 53%, and 42% CPS by mass; the remaining mass is protein carrier.

Because this sentence refers to "conjugates" and not a "conjugate", one can infer that the type Ia, II, and III conjugates are all separate and distinct molecules, and not attached to the same carrier protein, as recited in Applicants' claims.

This interpretation is further supported by an analysis of Section 2.1 of Michon '97 entitled "Preparation of Conjugate Vaccines" and the references cited therein. Nowhere does Section 2.1 state that the capsular polysaccharides are attached to the same carrier protein molecule. Moreover, references 3 and 5 of Michon '97, which were cited for a description of the methodology for producing the conjugates, do not disclose any method for conjugating multiple

capsular polysaccharides to the same carrier protein molecule [For the Examiner's convenience, copies of these articles have been submitted with this response.]

Because Michon '97 does not disclose all of the claim elements recited in Applicants' claims, Applicants respectfully assert that claims 1, 5, 6, 22, and 42-44 are not anticipated by Michon '97 under 35 U.S.C. § 102(b). Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

B. Rejection of Claims 1, 2, 5, 6, 10, 11, and 42-44 over Paoletti

Applicants' respectfully traverse the rejection of claims 1, 2, 5, 6, 10, 11, and 42-44 under 35 U.S.C. § 102(b) as allegedly being anticipated by Paoletti. Briefly, Paoletti does not disclose all of the claim elements of Applicants' claims. Accordingly, the rejection should be withdrawn. MPEP § 2131.

Paoletti is directed to a tetravalent GBS polysaccharide-tetanus toxoid conjugate vaccine. Similar to Michon '97, Paoletti does not disclose that different types of capsular polysaccharides can be conjugated to the same protein molecule. At best, it appears that Paoletti merely combines individual conjugates (which each contain one type of capsular polysaccharide attached to one type of protein molecule) to produce a trivalent or a tetravalent vaccine.

For example, with respect to the trivalent vaccine, Paoletti states that "[t]he GBS trivalent conjugate vaccine was composed of 2 μg each of Ia-TT, II-TT, and III-TT in a total volume of 0.3 ml of phosphate-buffered saline, pH 7.0 (PBS)" [Paoletti, page 3237, col. 1, last paragraph (emphasis added)]. Similarly, for the tetravalent vaccine, Paoletti states that "GBS tetravalent conjugate vaccine was made by combining the same three individually prepared

conjugates used in the trivalent GBS conjugate vaccine and the newly prepared Ib-TT vaccine" [Paoletti, page 3238, col. 2, first full paragraph, (emphasis added)].

Applicant does not see any disclosure in Paoletti that describes "[a] multivalent conjugate molecule comprising a carrier protein with at least three different bacterial capsular polysaccharides covalently linked to the carrier protein" as recited in Applicants' claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 2, 5, 6, 10, 11, and 42-44 under 35 U.S.C. § 102(b). See MPEP § 2131.

Rejections under 35 U.S.C. § 103

A. Rejection of Claims 9 and 52 over Paoletti, in view of Wang

Applicants respectfully traverse the rejection of claims 9 and 52 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Paoletti, in view of Wang. Briefly, the proposed combination of references fails to teach or suggest all of the elements of Applicants' claims. Accordingly, the rejection of these claims should be withdrawn. MPEP § 2143.

As noted above, Paoletti does not disclose a "multivalent conjugate molecule" as recited in Applicants' claims. At best, Paoletti merely describes the combination of individual conjugates in the preparation of trivalent or tetravalent vaccines.

Wang does not alleviate this deficiency of Paoletti, as Wang is directed to the use of ozonolysis to selectively depolymerize polysaccharides containing β-D-aldosidic linkages. Nowhere does Wang teach or suggest a "multivalent conjugate molecule" as recited in Applicants' claims.

Thus, Paoletti and Wang, whether taken alone or in combination, do not teach or suggest a "multivalent conjugate molecule" as claimed in Applicants' claims. Because the

proposed combination of references fails to teach or suggest all of the claim elements of Applicants' claims, the rejection should be withdrawn. MPEP § 2143.

B. The Rejection of Claims 2, 3, 7, 8, 45, and 46 over Michon '97, in view of Michon '508 and Laude-Sharp

Applicants respectfully traverse the rejection of claims 2, 3, 7, 8, 45, and 46 over Michon '97, in view of Michon '508 and Laude-Sharp. Briefly, none of the references, either alone or in combination, teach or suggest all of the claimed elements in Applicants' claims. Accordingly, the rejection under 35 U.S.C. § 103(a) should be withdrawn.

Michon '97 does not teach or suggest Applicants' claimed multivalent conjugate, but instead the combination of single polysaccharide-protein conjugates to form a multivalent vaccine. This was discussed above in connection with the rejection of claims 1, 5, 6, 22, and 42-44.

Michon '508 is directed to depolymerized Group B streptococcus type II and type III polysaccharides. While Michon '508 "contemplates multivalent conjugates and their vaccines wherein different types of polysaccharides are conjugated to a single protein" [Michon '508, col. 9, lines 38-40], Applicants respectfully note that Michon '508 does not teach or suggest Applicants' claimed multivalent conjugate, which includes "at least three different bacterial capsular polysaccharides [that] are purified bacterial capsular polysaccharides obtained by treating bacteria with an enzyme or base, directly followed by separation." Michon '508 describes the preparation of polysaccharides of type II and III Group B Streptococcus that includes three steps: (1) base treatment, (2) nitrosation and rearrangement to form a terminal 2,5-anhydro-D-mannose structure and (3) separation [e.g, see Michon '508, Example 1].

Nowhere does Michon '508 teach or disclose the preparation of type II or III Group B Streptococcus polysaccharides (or any other strain of bacteria) by "treating bacteria with an enzyme or base, directly followed by separation", as recited in Applicants' claim 1. Indeed, it appears that Michon '508 actually teaches away from the use of enzymes by describing enzymatic methods as "costly" [Michon '508, col. 2, line 11]. Accordingly, like Michon '97, Michon '508 also does not teach or suggest Applicants' claimed multivalent conjugate.

Laude-Sharp does not alleviate the deficiencies of Michon '97 or Michon '508. Laude-Sharp describes a "trivalent combination vaccine, consisting of CPS-Cβ conjugates derived from CPS types Ia, II, and III". Because Laude-Sharp describes combining "conjugates" to make the multivalent vaccine, one can infer that even though the vaccine is trivalent, the conjugates themselves are not. Thus, similar to Michon '97, Laude-Sharp does not teach or suggest Applicants' claimed multivalent conjugate.

Because all of the cited references, whether considered alone or in combination, fail to teach or suggest all of the claim elements of Applicants' invention, the rejection of claims 2, 3, 7, 8, 45, and 46 should be withdrawn. Applicants respectfully request reconsideration and withdrawal of the rejection of these claims.

C. Applicants' Claims Are Patentable Over Jennings, in view of Paoletti and Claesson

Applicants respectfully traverse the rejection of claims 1-7 and 42-45 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Jennings, in view of Paoletti and Claesson. None of these references, alone or in combination, teach or disclose Applicants' claimed multivalent conjugate. Accordingly, the rejection should be withdrawn. MPEP § 2143.

Jennings is directed to vaccines for type II and V Group B Streptococcus bacteria. Nowhere does Jennings teach or suggest Applicants' claimed multivalent conjugates. Instead, Jennings merely discusses multivalent vaccines that are prepared by combining conjugate molecules that have only one type of polysaccharide attached to a protein component. According to Jennings,

> this invention claims multivalent vaccines comprising the conjugate **molecules** of the invention and **at least one other immunogenic molecule** capable of eliciting the production of antibodies to a pathogenic substance other than Group B streptococcus type II or type V. In particular, in addition to comprising the GBS type II and/or GBS type V conjugate **molecules**, the multivalent vaccine, according to the invention, further comprises **other immunogenic molecules** capable of eliciting the production of antibodies to pathogens selected from the group consisting of Group B streptococcus types Ia, Ib, III, IV and Haemophilus influenzae type b and E. coli type K1 [Jennings, col. 2, lines 53-65].

Similarly, Paoletti does not teach or suggest the claimed multivalent conjugate either, for the reasons set forth above in connection with the 35 U.S.C. § 102(b) claim rejections based on Paoletti.

Claesson does not alleviate the deficiencies of Jennings or Paoletti, because Claesson does not teach or suggest the claimed multivalent conjugate either. At best, Claesson merely describes a Hib-TT conjugate that contains only one type of polysaccharide attached to a protein carrier.

Because all of the cited references, whether considered alone or in combination, fail to teach or suggest all of the claim elements of Applicants' invention, the rejection of claims 1-7 and 42-45 should be withdrawn. Applicants respectfully request reconsideration and withdrawal of the rejection of these claims.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 50-3732, Order No. 13564-105038US1.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-3732, Order No. 13564-105038US1.

Respectfully submitted,
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